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Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/032,254 | CHODOSH ET AL. | |
| | Examiner | Art Unit | |
| | Stephen L. Rawlings, Ph.D. | 1642 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *10 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) *1,2,5-38,41,43,45 and 47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,4,39,40,42,44 and 46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20021209*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Notice to Comply*.

## DETAILED ACTION

1. The election without traverse filed September 10, 2004 is acknowledged and has been entered.

Applicant has elected the invention of Group II, claims 3, 4, 39, 40, 42, 44, and 46, drawn to an isolated nucleic acid molecule, a vector comprising said nucleic acid molecule, and a cell comprising said nucleic acid molecule.

2. Claims 1-47 are pending in this application. Claims 1, 2, 5-38, 41, 43, 45, and 47 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on September 10, 2004.

3. Claims 3, 4, 39, 40, 42, 44, and 46 are currently under prosecution.

### *Information Disclosure Statement*

4. The information disclosure filed December 9, 2002 has been considered. An initialed copy is enclosed.

### *Priority*

5. Applicant's claim under 35 USC § 119(e) for benefit of the earlier filing date of US Provisional Application No. 60/257,073, filed December 21, 2000, is acknowledged. However, the present claims are not entitled to the claimed benefit of the earlier filing date of this provisional application for the following reasons:

Claim 3 is drawn to a nucleic acid molecule encoding "Pnck", a cancer-linked protein kinase. The representative embodiment of "Pnck", which is

disclosed in the instant application, comprises the amino acid sequence set forth as SEQ ID NO: 2. US Provisional Application No. 60/257,073 fails to adequately describe the presently claimed nucleic acid molecule encoding "Pnck", which is presently disclosed as having the amino acid sequence set forth as SEQ ID NO: 2, to meet the enablement and written description requirements set forth under 35 USC § 112, first paragraph, because the "Pnck" polypeptide described in the provisional application comprises an amino acid sequence that differs from SEQ ID NO: 2; see Figure 2B of the provisional application.

Claim 4 is drawn to the nucleic acid molecule of claim 3, which comprises the polynucleotide sequence set forth as SEQ ID NO: 1. US Provisional Application No. 60/257,073 fails to adequately describe the presently claimed nucleic acid molecule having the polynucleotide sequence set forth as SEQ ID NO: 1 to meet the enablement and written description requirements set forth under 35 USC § 112, first paragraph, because the nucleic acid molecule encoding the "Pnck" polypeptide, which is described in the provisional application, comprises a polynucleotide sequence that differs from SEQ ID NO: 1; see Figure 2A of the provisional application.

Claim 42 is drawn to a nucleic acid molecule comprising a polynucleotide sequence that is complementary to all or part of the polynucleotide sequence of the nucleic acid molecule of claim 3, a mutant thereof, a derivative thereof, a homologue thereof, or a fragment thereof encoding "a cell [sic] having Pnck activity". Again, US Provisional Application No. 60/257,073 fails to adequately describe the presently claimed nucleic acid molecule encoding "Pnck", which is presently disclosed as having the amino acid sequence set forth as SEQ ID NO: 2, to meet the enablement and written description requirements set forth under 35 USC § 112, first paragraph, because the "Pnck" polypeptide described in the provisional application comprises an amino acid sequence that differs from SEQ ID NO: 2; but moreover, the provisional application fails to adequately describe mutants, derivatives, homologues, and fragments of the such nucleic acid molecules that encode polypeptides having "Pnck activity".

Claims 39 and 44 are drawn to a recombinant cell or a mammalian cell comprising the nucleic acid molecules of claim 3 or claim 42. While US Provisional Application No. 60/257,073 fails to adequately describe the presently claimed nucleic acid molecules of clams 3 and 42 for the reasons set forth above, it is further noted that the provisional application fails to adequately describe recombinant cells and mammalian cells that comprise such nucleic acid molecules.

Claims 40 and 46 are drawn to nucleic acid molecules, or more specifically to vectors, which comprise the polynucleotide sequence of the nucleic acid molecule of claim 3; however, US Provisional Application No. 60/257,073 fails to adequately describe the presently claimed invention to meet the written description requirements set forth under 35 USC § 112, first paragraph, because, while the provisional application does not describe the nucleic acid molecule of claim 3, it also does not describe vectors comprising such polynucleotide sequences (claim 40) or such nucleic acid molecules operably fused to a reporter gene or a fragment thereof (claim 46).

Accordingly, the earliest effective filing date of present claims 3, 4, 39, 40, 42, 44, and 46 is considered the filing date of the instant application, namely December 21, 2001.

***Specification***

6. The disclosure is objected to for the following reason: The specification contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). Sequences appearing in the specification and/or drawings must be identified by sequence identifier in accordance with 37 C.F.R. 1.821(d). According to 37 CFR § 1.821(a), an unbranched sequence of four or more specifically identified amino acids or an unbranched sequence of ten or more

nucleotides must be identified by sequence identification numbers. See MPEP § 2422.01.

In this instance, the sequences depicted in Figure 1 are not identified by sequence identification numbers, either in the figure or in the brief description of figure at page 7.

Applicant must provide appropriate amendments to the specification or drawings inserting the required sequence identifiers. Sequence identifiers for sequences appearing in the drawings may appear in the drawings or in the brief description of the drawings.

As noted in the attached Notice to Comply, appropriate action correcting this deficiency is required. If necessary to correct the deficiency, Applicant must submit paper and computer-readable copies of a substitute sequence listing, together with a statement that the content of both copies are the same and, where applicable, include no new matter.

7. The specification is objected to because the use of improperly demarcated trademarks has been noted in this application. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks. See MPEP § 608.01(v).

Examples of improperly demarcated trademarks include GenBank™ (page 11, paragraph 3), MacVector™ (page 31, paragraph 4), and SeaKem™ (page 32, paragraph 1).

Appropriate correction is required. Each letter of a trademark should be capitalized or otherwise the trademark should be demarcated with the appropriate symbol indicating its proprietary nature (e.g., ™, ®), and accompanied by generic terminology. Applicants may identify trademarks using the "Trademark" search engine under "USPTO Search Collections" on the Internet at http://www.uspto.gov/web/menu/search.html.

8. The disclosure is objected to because the disclosure refers to embedded hyperlinks and/or other forms of browser-executable code and to the Internet contents so identified. Reference to hyperlinks and/or other forms of browser-executable code and to the Internet contents so identified is impermissible and therefore requires deletion.

An example of such an impermissible disclosure appears at page 38 in paragraph 1.

The attempt to incorporate essential or non-essential subject matter into the patent application by reference to a hyperlink and/or other forms of browser-executable code is considered to be an improper incorporation by reference. See MPEP § 608.01(p), paragraph I regarding acceptable incorporation by reference. See 37 CFR § 1.57.

9. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR § 1.75(d)(1) and MPEP § 608.01(o).

The specification fails to provide antecedent basis for a nucleic acid sequence encoding Pnck, which further comprises a reporter gene, or a fragment thereof having reporter activity, operably fused to said nucleic acid sequence, as recited in claim 46. At present, other than in claim 46, none of the subject matter claimed is described in the specification; more particularly, there is no disclosure of a reporter gene or a functional fragment thereof, or a fusion consisting the nucleotide sequences encoding Pnck, or any other protein, and such a reporter gene or fragment thereof.

Appropriate correction is required.

***Claim Objections***

10. Claims 39, 40, and 46 are objected to because of the use of inconsistent phraseology and terminology. Claims 39, 40, and 46, which each depend from

claim 3, recite "the isolated nucleic acid of claim 3"; however, claim 3 is drawn to an isolated *nucleotide sequence*, rather than an isolated nucleic acid. Appropriate correction or rebuttal is required.

### *Claim Rejections - 35 USC § 101*

11. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

12. Claims 39 and 44 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 39 and 44 are broadly interpreted to encompass mammalian cells, which are not isolated and are comprised within an organism. Support for this interpretation of the claims can be found throughout the specification; see, e.g., page 5, paragraphs 3 and 5; page 7, paragraph 1; page 21, paragraph 2; and claims 16 and 47. Thus, the claims encompass cells that have been transfected with a polynucleotide encoding "Pcnk", which are comprised within a nonhuman or human animal, including humans treated using gene therapy.

MPEP § 2105 [R-1] states:

> If the broadest reasonable interpretation of the claimed invention as a whole encompasses a human being, then a rejection under 35 U.S.C. 101 must be made indicating that the claimed invention is directed to nonstatutory subject matter.

With particular regard to claim 39, although it is noted that the claim is specifically drawn to a "recombinant" cell, the Merriam-Webster's Online Dictionary, 10th Edition (copyright © 2005 by Merriam-Webster, Inc.), which is available on the Internet at http://www.m-w.com/, defines the term "recombinant" as "relating to or containing recombinant DNA"; therefore, because the specification discloses that the claimed recombinant cell can be produced by delivering the polynucleotide sequence encoding the protein kinase to a cell of which an animal, including a human, is comprised, the claimed recombinant cell

cannot be distinguished from a recombinant cell of which a human being is comprised produced using by such a process and accordingly, the claim encompasses non-statutory subject matter.

This issue can be remedied by amending claims 39 and 44 to recite, "isolated", before "recombinant cell" and "mammalian cell", respectively.

### *Claim Rejections - 35 USC § 112*

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 3, 39, 40, 42, 44, and 46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a written description rejection.

The considerations that are made in determining whether a claimed invention is supported by an adequate written description are outlined by the published Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, para. 1, ``Written Description'' Requirement (Federal Register; Vol. 66, No. 4, January 5, 2001). A copy of this publication can be viewed or acquired on the Internet at the following address: <http://www.gpoaccess.gov/>.

Claims 3, 39, 40, 42, 44, and 46 are directed nucleic acid molecules encoding "Pnck", as recited in claim 1. "Pnck", according to claim 1, is "a cancer-linked protein kinase".

The specification does not appear to explicitly define "Pnck" as the polypeptide of SEQ ID NO: 2, nor as the polypeptide encoded by the

polynucleotide sequence of SEQ ID NO: 1. Moreover, the use of such nomenclature alone does not serve to define the genus of polypeptides to which the claims are directed, since, for example, the italicized term "*Pnck*", which designates the gene encoding a "Pnck" polypeptide, can be found in reference to the genes found in both murine and human tissues. Furthermore, the specification contemplates homologues, analogs, derivatives, and fragments of "Pnck", which have "Pnck activity"; see, e.g., page 7, paragraph 1; page 15, paragraph 2, through page 16, paragraph 2; and claim 42. For example, the specification discloses that the present invention provides such analogs, which "can differ from naturally occurring proteins or peptides by conservative amino acid sequence differences or by modification that do not affect sequence, or by both" (page 15, paragraph 2).

Claims 3, 39, 40, 42, 44, and 46 are therefore broadly interpreted as though directed to a genus of nucleic acid molecules encoding a member of a genus of "Pnck" polypeptides, which includes but is not limited to the polypeptide of SEQ ID NO: 2.

Because the genus of "Pnck" polypeptides encoded by the claimed nucleic acid molecules includes homologues, analogs, derivatives, and fragments of "Pnck", which have "Pnck activity", where "Pnck activity" is not explicitly defined nor limited to the specific kinase activity of the polypeptide of SEQ ID NO: 2 (see, e.g., page 20, paragraph 4), the genus is considered to be composed of members that vary substantially in structure and function, as compared to the polypeptide of SEQ ID NO: 2. Moreover, the specification does not disclose a correlation between any one particularly identifying structural feature of the polypeptide of SEQ ID NO: 2, which is shared by most other members of the genus of "Pnck" polypeptides, and any specific functional feature, which is also common among at least most of the otherwise structurally different members. For example, the specification does not describe which amino acid residues of the polypeptide of SEQ ID NO: 2 are essential to any one particular activity of the polypeptide, which must be retained by the other members of the genus of

"Pnck" polypeptides having the same activity. Therefore, the polypeptide of SEQ ID NO: 2 is not deemed representative of at least most of the members of the genus of "Pnck" polypeptides; and it follows that the nucleic acid molecule of SEQ ID NO: 1 is not properly considered representative of the genus of claimed nucleic acid molecules encoding such disparate polypeptides.

Because the polynucleotide sequence of SEQ ID NO: 1 is not representative of the claimed genus of nucleic acid molecules, absent a detailed description of at least most of the members of the genus of molecules encoding the "Pnck" polypeptides, the skilled artisan could not immediately envision, recognize, or distinguish at least a substantial number of the members of the claimed genus of nucleic acid molecules. Therefore, the specification would not reasonably convey to the skilled artisan that Applicant had possession of the claimed invention at the time the application was filed.

*The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, ``Written Description" Requirement* (66 FR 1099-1111, January 5, 2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). The *Guidelines* further state, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species *cannot* be achieved by disclosing only one species within the genus" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus. Because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant

was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant had possession of the claimed invention at the time the application was filed.

15. Claims 3, 39, 40, 42, 44, and 46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making and using nucleic acid molecules disclosed by the prior art, which encode cancer-associated protein kinases, and a nucleic acid molecule comprising the polynucleotide sequence of SEQ ID NO: 1 or a nucleic acid molecule encoding a polypeptide having the amino acid sequence set forth as SEQ ID NO: 2 and a vector and isolated host cell comprising such a nucleic acid molecule, does not reasonably provide enablement for a nucleic acid molecule encoding any "Pnck" polypeptide, including any homologues, analogs, derivatives, and fragments thereof that have "Pnck activity", or a vector and isolated host cell comprising such a nucleic acid molecule. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This is a scope of enablement rejection.

The amount of guidance, direction, and exemplification disclosed by Applicant would not be sufficient to enable the skilled artisan to use the claimed invention without a need to perform an undue amount of additional experimentation.

Factors to be considered in determining whether undue experimentation is required are summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986). These factors include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in

the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The specification teaches the polypeptide of SEQ ID NO: 2 is encoded by an isolated nucleic acid molecule comprising the polynucleotide sequence set forth as SEQ ID NO: 1; see, e.g., Figure 1. In addition, the specification teaches the human homologue of the polypeptide of SEQ ID NO: 2, which comprises the amino acid sequence set forth as SEQ ID NO: 8 and is encoded by an isolated nucleic acid molecule comprising the polynucleotide sequence set forth as SEQ ID NO: 7; see, e.g., page 12, paragraph 2.

However, as explained above, claims 3, 39, 30, 42, 44, and 46 are broadly interpreted as though directed to a genus of nucleic acid molecules encoding a member of a genus of "Pnck" polypeptides, which includes but is not limited to the polypeptide of SEQ ID NO: 2. Because the term "Pnck" is not defined in a limiting manner, the claims are reasonably interpreted to encompass nucleic acid molecules encoding any cancer-linked protein kinase. The genus of "Pnck" polypeptides to which claims are directed is considered to be composed of members that vary substantially in structure and function, as compared to the polypeptide of SEQ ID NO: 2, since cancer-associated protein kinases are known to vary markedly in both structure and function.

Claims 42 and 44 are directed to nucleic acid molecules encoding a member of a genus of "Pnck" polypeptides that includes homologues, analogs, derivatives, and fragments of "Pnck", which have "Pnck activity"; however, "Pnck activity" is not explicitly defined nor limited to the specific kinase activity of the polypeptide of SEQ ID NO: 2 or its functional expression. Therefore, the genus of "Pnck" polypeptides to which claims 42 and 44 are directed is considered to be composed of members that vary substantially in structure and function, as compared to the polypeptide of SEQ ID NO: 2, and are not necessarily cancer-linked protein kinases.

The prior art teaches nucleic acid molecules that encode cancer-associated protein kinases, which absent a showing of any difference, are deemed the same as those that are claimed in the instant application. For example, Kiley et al. (*J. Mammary Gland Biol. Neoplasia.* 1996 Apr; **1** (2): 177-187) teaches protein kinase C isozymes, which are linked to cancer; see entire document (e.g., the abstract).

One cannot make that which has not been fully described in structural and functional detail. Although methods for isolating other nucleic acid molecules encoding polypeptides that are structurally related to the polypeptide of SEQ ID NO: 2 are conventional in the art, the skilled artisan cannot distinguish such polypeptides that have the same function as the polypeptide of SEQ ID NO: 2 from others, because the particular biological function of the polypeptide of SEQ ID NO: 2 has not been described. Similarly, although methods for isolating other kinases are conventional in the art, the skilled artisan cannot distinguish polypeptides that function in the same manner as the polypeptide of SEQ ID NO: 2 from others, again, because the particular biological function of the polypeptide of SEQ ID NO: 2 has not been described.

If the claimed nucleic acid molecules are not taught by the prior art and do not encode a polypeptide that is functionally equivalent to the polypeptide of SEQ ID NO: 2 (e.g., phosphorylates the same pool of substrates or is associated with the same disease by its overexpression in affected cells), the skilled artisan would be left to evaluate the function or activity of the polypeptides before using their use, which would constitute a need to first perform an undue amount of additional experimentation. Not all "Pnck" polypeptides, even those that are substantially homologous to the polypeptide of SEQ ID NO: 2, are reasonably expected to have the same or similar function.

Skolnick et al. (*Trends in Biotechnology* **18**: 34-39, 2000), for example, discloses that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (see, e.g., the

abstract; and page 34, *Sequence-based approaches to function prediction*). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see, in particular, the abstract and Box 2).

In addition, Bowie et al. (*Science* **257**: 1306-1310, 1990) teaches that an amino acid sequence encodes a message that determines the shape and function of a protein; and, that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome. Bowie et al. teaches that the determination of protein structure from sequence data and, in turn, utilizing structural determinations to ascertain functional aspects of the protein is extremely complex (page 1306, column 1). Even if the skilled artisan were able to submit a complete list of the possible nucleic acids and the proteins encoded thereby, which fall within the scope of the claims, the skilled artisan could not recognize which of these would function similarly to a protein comprising SEQ ID NO: 2, and which would not.

Thus, one skilled in the art would not accept the assertion, which is based only upon an observed similarity in amino acid sequence, that a variant of the polypeptide of SEQ ID NO: 2 is capable of functioning the same, or even as having the same structure as the polypeptide of SEQ ID NO: 2.

Although the polypeptide of SEQ ID NO: 2 is disclosed as having kinase activity, the specification does not describe which amino acid residues of the polypeptide of SEQ ID NO: 2 are essential to that activity and which must be retained by other members of the genus of "Pnck" polypeptides to have the same activity. Moreover, the specification does not teach which other amino acid residues can replace such functionally and/or structurally essential amino acids without a loss of that activity. Furthermore, although the polypeptide of SEQ ID NO: 2 is disclosed as having kinase activity, the specification does not describe the other proteins that are its substrates and the pool of substrates upon which kinases act largely defines their specific functions. Again, as evidenced by the

teachings of Skolnick et al. and Bowie, for example, the skilled artisan cannot accurately and reliably predict whether a given homologue of a particular protein known to have a certain activity will also have that activity. The more structurally disparate a given protein, the less likely the protein will share the function of structurally related proteins having known functions. Burgess et al. (*Journal of Cell Biology* **111**: 2129-2138, 1990) exemplifies the sensitivity of proteins to alterations of even a single amino acid in a sequence. Burgess et al. teaches that replacement of a single lysine reside at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. As another example of this sensitivity to amino acid sequence variations, Lazar et al. (*Molecular and Cellular Biology*, 1988, **8**: 1247-1252) teaches that a replacement of aspartic acid at position 47 with alanine or asparagine in transforming growth factor alpha had no effect but that a replacement with serine or glutamic acid sharply reduced its biological activity. Thus, Lazar et al. teaches that even a single *conservative* type amino acid substitution may adversely affect the function of a protein.

In conclusion, upon careful consideration of the factors used to determine whether undue experimentation is required, in accordance with *Ex parte Forman*, 230 USPQ 546 (BPAI 1986), the amount of guidance, direction, and exemplification disclosed by Applicant is not deemed sufficient to enable the skilled artisan to use the claimed invention without a need to perform an undue amount of additional experimentation.

16. Claims 39 and 44 are further rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making and using an **isolated** recombinant cell, including an isolated recombinant mammalian cell, comprising a nucleic acid molecule comprising the polynucleotide sequence of SEQ ID NO: 1 or a nucleic acid molecule encoding a polypeptide having the amino acid sequence set forth as SEQ ID NO: 2, does not reasonably provide enablement for making and using any recombinant cell comprising such a nucleic

acid molecule. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claim 39 is drawn to a recombinant cell comprising a nucleic acid molecule according to claim 3, which comprises a polynucleotide sequence encoding "Pnck". The claim is broadly interpreted to encompass host cells, which are not isolated and are comprised within an organism. Thus, the claim encompasses host cells that have been transfected with a nucleic acid molecule encoding "Pnck" that are comprised within an animal, including nonhuman or human animals, treated using gene therapy.

Similarly, claim 44 is drawn to a mammalian cell comprising a recombinant nucleic acid molecule comprising a polynucleotide sequence that is complementary to a nucleic acid sequence encoding "Pnck", a mutant thereof, a derivative thereof, a homologue thereof, or a fragment thereof having "Pnck activity". Therefore, claim 44 also encompasses host cells that have been transfected with a nucleic acid molecule encoding "Pnck" that are comprised within an animal, including nonhuman or human animals, treated using gene therapy.

The teachings of the specification cannot be extrapolated to the enablement of the claimed invention because the amount of guidance, direction, and exemplification set forth therein would not be sufficient to enable the skilled artisan to make and use the claimed invention without the need to perform an undue amount of additional experimentation.

Again, the factors to be considered in determining whether undue experimentation is required are summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986). These factors include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the

quantity of experimentation which would be required in order to practice the invention as claimed.

The specification discloses that nucleic acid molecules and vectors encoding the polypeptide of SEQ ID NO: 2 (i.e., Pnck) can be used to produce medicaments and pharmaceutical compositions, which can be administered to patients to treat diseases by gene therapy; see, e.g., page 5, paragraphs 3 and 5, page 21, paragraph 2, and claim 16. Furthermore, the specification contemplates transgenic animals that recombinantly express the polypeptide encoded by the claimed nucleic acid molecules; see, e.g., page 7, paragraph 1, and claim 47.

The specification does not provide a sufficient amount of guidance, direction, or exemplification to enable the skilled artisan to make or use host cells that are comprised within a non-human transgenic animal. In the art of producing transgenic animals, the phenotype of the resultant transgenic animal is not always predictable; nor is the transgenic embryo always viable. Houdebine (*Journal of Biotechnology* 1994, 34: 269-287) teaches the vectors to be used for directing the expression of transgenes in any given tissue, or in all tissues, must contain the appropriate regulatory regions; see entire document (e.g., paragraph bridging pages 272 and 273). Houdebine teaches expression is heavily dependent on the site of integration in the host genome and the site of integration is presently unpredictable (page 27, column 1). Therefore, it is concluded that one of skill in the art would need to perform an undue amount of experimentation in order to make and use the claimed host cell comprised within a transgenic animal.

In addition, the specification does not teach provide a sufficient amount of guidance, direction, and exemplification to enable the skilled artisan to have a reasonable expectation of successfully producing the claimed host cells within a living organism by gene transfer, or *gene therapy*. The art of gene therapy, i.e., the *in vivo* delivery genetic information to targeted cells within a body using naked DNA or viral vectors or by reintroducing *ex vivo* modified host cells into the

body, is still in its infancy. Moreover, the art is highly unpredictable and its successful application has been hindered by numerous limitations, which the specification does not remedy and would preclude the skilled artisan from having a reasonable expectation of successfully making and using the claimed invention without need of performing an undue amount of experimentation.

For example, the teachings of the specification have not overcome the problems with *in vivo* delivery and expression. Verma et al. (*Nature* 1997, **389**: 239-242) teaches that the Achilles heel of gene therapy is gene delivery (page 239, column 3). Verma et al. states that the ongoing problem is the inability to deliver genes efficiently and to obtain sustained expression; see entire document (e.g., page 239, column 3). Similarly, Amalfitano et al. (*Current Gene Therapy* 2002, **2**: 111-133) teaches that non-viral mediated transfer of DNA generally suffers from low transduction efficiencies; see entire document (e.g., page 111, column 2). In addition, Amalfitano et al. discusses numerous limitations that have been encountered in using retroviral vectors to deliver DNA into a subject and teaches the use of adenoviral vectors can be ineffective because of the induction of strong immune responses in the host to the viral vectors and direct acute and chronic toxicity caused by the vector itself; see entire document (e.g., abstract).

It is noted that Amalfitano et al. teaches that a despite general lack of success, the first conclusive evidence that gene therapy can show efficacy in humans was achieved in human X-linked SCID subjects *via* retrovirus transduction (page 111, column 2). However, since the publication, The Department of Health and Human Services has released a memorandum dated January 14, 2003, a copy of which is attached to this Office action, that urges all such investigations to be discontinued until new data are available, the possible etiology and risks of adverse events associated are considered, and recommendations emerge. Despite the initial promise of the trial studying gene transfer as a possible treatment for the disease, investigators have found that retroviral-mediated insertion of the transgene has caused the subjects to develop

cancer. The results of the trial underscore the high degree of unpredictability associated with the art and the fact that the skilled artisan could not make or use the claimed invention with a reasonable expectation of success without need to perform additional and an undue amount of experimentation.

The state of the art, as a whole, is well defined by Pandha et al. (*Current Opinion in Investigational Drugs* 2000; **1** (1): 122-134). Pandha et al. teaches:

> Despite the rapid technological advances that continue to sustain the field of cancer gene therapy, few individual patients have benefited from the revolution so far. The plethora of clinical trials described confirms that each malignancy will have its own ideal strategy based on the associated molecular defects, and there has been rapid progress from this viewpoint. At the same time, there has been a renewed appreciation for the limitations to gene therapy, which include low efficiency of gene transfer, poor specificity of response and methods to accurately evaluate responses, and lack of truly tumor-specific targets at which to aim. As with all new therapies, we are climbing a steep learning curve in terms of encountering treatment-related toxicities, as well as profound ethical and regulatory issues (abstract).

In view of the preponderance of evidence establishing the state of the art, now and at the time the application was filed, and the level of unpredictability associated therewith, in the absence of a disclosure of an amount of guidance, direction, and exemplification that is reasonably commensurate in scope with the claims, it appears that skilled artisan could not make and use the claimed invention with a reasonable expectation of success without having the need to perform an undue amount of experimentation.

This issue can be remedied by amending claims 39 and 44 to recite, "isolated", before "recombinant cell" and "mammalian cell", respectively.

17. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

18. Claims 42, 44, and 46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 42 and 44 are indefinite because claim 42 recites, "encoding a cell having Pnck activity". Because mutants, derivatives, homologues, and fragments

of all or part of the nucleic acid sequence of claim 3 do not encode *a cell*, but rather might encode a polypeptide, the metes and bounds of the subject matter that Applicant regards as the invention cannot be determined.

Claim 44 is also indefinite because the claim recites, "the recombinant nucleic acid molecule according to claim 42". There is no antecedent basis in claim 42 to support the recitation of this limitation in claim 44; therefore, the metes and bounds of the subject matter that Applicant regards as the invention cannot be determined.

Claim 46 is indefinite because the claim recites "fused thereto". Claim 46 is drawn to the isolated nucleic acid molecule of claim 3, which is drawn to an isolated nucleotide sequence encoding a purified cancer-linked protein kinase, Pnck. Claim 46 further limits the subject matter of claim 3 by reciting that the nucleic acid molecule of claim 3 comprises a reporter gene, or a fragment thereof having reporter activity, operably fused thereto; however, one would not ordinarily describe a nucleic acid molecule comprising a reporter gene or fragment thereof as "operably fused" to itself, but perhaps to another sequence component of which the molecule is comprised. Furthermore, it is aptly noted that the artisan would not typically "operably fuse" a reporter gene to a polynucleotide sequence encoding a protein, such as a kinase; rather a reporter gene is typically said to be "operably fused" to a promoter, such that the resultant construct can be used, for example, to study the factors that regulate the activity of the promoter by measuring the level of expression of the reporter gene. Albeit atypical, were the reporter gene of the nucleic acid molecule "operably fused" to a polynucleotide sequence encoding a protein, the artisan would not understand how and why, because it would not be understood of what operation the fusion must be capable, and so, it could not be ascertained how such a fusion must be made. One might fuse the polynucleotide sequence encoding a protein to another sequence encoding a reporter (e.g., green fluorescent protein), but the artisan would not ordinarily describe such a fusion as "operable"; rather the artisan would typically describe such a fusion of one sequence to the other as

"in-frame", indicating that the resultant construct has the capability of encoding a fusion protein comprised of the amino acid sequence encoded by the first sequence adjoined to the amino acid sequence encoded by the second sequence without generating a missense or truncating mutation in the latter. Accordingly, while claim 46 is drawn to a nucleic acid molecule comprising an isolated nucleotide sequence encoding a purified cancer-linked protein kinase and a reporter gene or fragment thereof, the metes and bounds of the subject matter that Applicant regards as the invention cannot be determined, because it cannot be determined to what subject matter the reporter gene or fragment thereof is operably fused.

***Claim Rejections - 35 USC § 102***

19. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

20. Claims 3, 4, 39, 40, and 42 are rejected under 35 U.S.C. 102(b) as being anticipated by Gardner et al. (*Genomics*. 2000 Jan 15; **63** (2): 279-288), as evidenced by the USPTO search report "us-10-032-254a-1.rge", pages 1 and 2 of the "Alignments" (result 1) and Lehninger et al. (Principles of Biochemistry, 2nd Ed., Worth Publishers: New York, 1993, pages 984-995).

Claims 3 and 4 are drawn to a nucleic acid molecule comprising the nucleotide sequence set forth as SEQ ID NO: 1, which encodes cancer-linked protein kinase, Pnck. Claim 39 is drawn to a recombinant cell comprising the nucleic acid of claim 3. Claim 40 is drawn to a vector comprising a nucleotide sequence that encodes cancer-linked protein kinase, Pnck. Claim 42 is drawn to a nucleic acid molecule that comprises a polynucleotide sequence that is

complementary to all or part of a nucleic acid sequence encoding cancer-linked protein kinase, Pnck.

USPTO search report "us-10-032-254a-1.rge", pages 1 and 2 of the "Alignments" (result 1), which was generated using SEQ ID NO: 1 as a query in searching GenBank™, shows that SEQ ID NO: 1 is identical to the polynucleotide sequence that has been reported as GenBank™ Accession No. AF181984.

Lehninger et al. teaches conventional recombinant DNA methodology, including that which is used to produce and screen cDNA libaries to isolate a nucleic acid molecule encoding a particular protein of interest; see the entirety of pages 984-995 (e.g., page 986, Figure 28-1). In addition, Lehninger et al. teaches that cDNA molecules are double-stranded DNA molecules comprised of two DNA strands, each having a polynucleotide sequence that fully complementary to the other; see, e.g., page 994, Figure 28-9.

As evidenced by the USPTO search report, Gardner et al. discloses an isolated nucleic acid molecule comprising a polynucleotide sequence that is identical to the polynucleotide sequence set forth as SEQ ID NO: 1; see entire document (e.g., page 282, Figure 1). Gardner et al. discloses that this polynucleotide sequence has been reported as GenBank™ Accession No. AF181984 (page 280, column 2). Gardner et al. further discloses that this polynucleotide sequence encodes protein kinase, Pnck (see, e.g., the abstract), which absent a showing of any difference is deemed the same as the cancer-linked protein kinase, Pnck, to which the claims are directed. In addition, Gardner et al. teaches the polynucleotide sequence was determined by isolating a lambda phage (i.e., a vector) comprising a nucleic acid molecule having the polynucleotide sequence from a cDNA library; see, e.g., page 280, column 2. As evidenced by Lehninger et al., the isolated vector thus comprises a double-stranded DNA molecule comprising a sequence that is complementary to all of the polynucleotide sequence encoding the kinase.

Although Gardner et al. does not explicitly disclose a recombinant cell comprising the nucleic acid molecule having the polynucleotide sequence was

produced, as evidenced by Lehninger et al., the conventional methodology described by Gardner et al., which was used to isolate the nucleic acid molecule, necessarily involves at least one step in which a recombinant cell comprising the nucleic acid molecule is produced. Therefore, although Gardner et al. does not explicitly disclose such a recombinant cell, it is implicit, as would be recognized by the artisan, that the reference teaches the production and use of a host cell comprising a nucleic acid molecule having the polynucleotide sequence.

21. Claims 3, 39, 40, 42, 44, and 46 are rejected under 35 U.S.C. 102(b) as being anticipated by Shirai et al. (*Jpn. J. Pharmacol.* 1998 Dec; **78** (4) :411-417), as evidenced by Kiley et al. (*J. Mammary Gland Biol. Neoplasia.* 1996 Apr; **1** (2): 177-187) and Lehninger et al. (Principles of Biochemistry, 2nd Ed., Worth Publishers: New York, 1993, pages 984-995).

Herein, claim 3 is drawn to a nucleic acid molecule that encodes a cancer-linked protein kinase. Although the claim identifies the genus of such polypeptides by the nomenclature "Pnck", as noted above, "Pnck" is not explicitly defined in a limiting manner in the specification, such that the claimed subject matter is clearly understood to be limited to a nucleic acid molecule comprising the polynucleotide sequence of SEQ ID NO: 1 or to a nucleic acid molecule encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2 or a substantially similar polypeptide. Accordingly, claims 39 and 44 are drawn to a recombinant mammalian cell comprising a nucleic acid molecule that encodes a cancer-linked protein kinase. Claim 40 is drawn to a vector comprising a nucleotide sequence that encodes a cancer-linked protein kinase. Claim 42 is drawn to a nucleic acid molecule that comprises a polynucleotide sequence that is complementary to all or part of a nucleic acid sequence encoding a cancer-linked protein kinase. Claim 46 is drawn to a "fused" nucleic acid molecule comprising a polynucleotide sequence encoding a cancer-linked protein kinase adjoined to a polynucleotide sequence encoding a "reporter" polypeptide.

Kiley et al. teaches protein kinase C (PKC) isozymes are linked to cancer; see entire document (e.g., the abstract).

Lehninger et al. teaches that cloned DNA molecules of which plasmids are comprised are double-stranded DNA molecules comprised of two DNA strands, each having a polynucleotide sequence that fully complementary to the other; see the entirety of pages 984-995 (e.g., page 994, Figure 28-9).

As evidenced by Kiley et al., Shirai et al. teaches a nucleic acid molecule comprising a polynucleotide sequence encoding a cancer-linked protein kinase, namely protein kinase C (PKC), and a polynucleotide sequence encoding a "reporter" polypeptide, namely green fluorescent protein (GFP); see entire document (e.g., the abstract). Shirai et al. teaches the fused nucleic acid molecule encodes a fusion protein comprising the amino acid sequence of protein kinase C adjoined to the amino acid sequence of GFP; see, e.g., the abstract. Shirai et al. teaches a mammalian host cell comprising the nucleic acid molecule; see, e.g., the abstract. As evidenced by Lehninger et al. the nucleic acid constructs disclosed by Shirai et al., which encode PKC, are double-stranded and therefore comprise a nucleic acid molecule comprising a polynucleotide sequence fully complementary to the polynucleotide sequence encoding the kinase.

22. Claim 3 is rejected under 35 U.S.C. 102(b) as being anticipated by Database GenBank™ Accession No. AB023027 (04 December 1999), as evidenced by the USPTO search report "us-10-032-254a-2.rge", pages 1 and 2 of the "Alignments" (result 1).

Claim 3 is drawn to a nucleic acid molecule that encodes a cancer-linked protein kinase, "Pnck". The instant specification teaches an embodiment of the claimed invention, which is a nucleic acid molecule comprising a polynucleotide sequence that encodes a "Pnck" polypeptide that comprises the amino acid sequence set forth as SEQ ID NO: 2. Therefore, claim 3 is interpreted herein as

encompassing a nucleic acid molecule encoding a polypeptide comprising the amino acid sequence set forth as SEQ ID NO: 2.

USPTO search report "us-10-032-254a-2.rge", pages 1 and 2 of the "Alignments" (result 1), which was generated using SEQ ID NO: 2 as a query in searching GenBank™, shows that SEQ ID NO: 2 is identical to the amino acid sequence of a polypeptide encoded by a polynucleotide sequence that has been reported as GenBank™ Accession No. AB023027.

As evidenced by the USPTO search report, Database GenBank™ Accession No. AB023027 discloses the polynucleotide sequence of an isolated nucleic acid molecule comprising a polynucleotide sequence that encodes a polypeptide having an amino acid sequence that is identical to the amino acid sequence set forth as SEQ ID NO: 2.

***Claim Rejections - 35 USC § 103***

23. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

24. Claims 44 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gardner et al. (*Genomics*. 2000 Jan 15; **63** (2): 279-288), as evidenced by the USPTO search report "us-10-032-254a-1.rge", pages 1 and 2 of the "Alignments" (result 1) and Lehninger et al. (Principles of Biochemistry, 2nd Ed., Worth Publishers: New York, 1993, pages 984-995) in view of Shirai et al. (*Jpn. J. Pharmacol.* 1998 Dec; **78** (4) :411-417), as evidenced by Kiley et al. (*J. Mammary Gland Biol. Neoplasia.* 1996 Apr; **1** (2): 177-187).

Claim 44 is drawn to a mammalian cell comprising a nucleic acid molecule according to claim 42; and herein, claim 46 is drawn to a "fused" nucleic acid

molecule comprising a polynucleotide sequence of SEQ ID NO: 1 encoding a "Pnck" polypeptide adjoined to a polynucleotide sequence encoding a "reporter" polypeptide.

As evidenced by the search report and Lehninger et al., Gardner et al. teaches that which is set forth above in the rejection of claims 3, 4, 39, 40, and 42 under 35 U.S.C. § 102(b).

Gardner et al. does not expressly teach a mammalian cell comprising a nucleic acid molecule comprising the disclosed polynucleotide sequence encoding the "Pnck" polypeptide (claim 44); nor does Gardner et al. expressly teach a "fused" nucleic acid molecule comprising a polynucleotide sequence encoding the "Pnck" polypeptide adjoined to a polynucleotide sequence encoding a "reporter" polypeptide (claim 46).

As evidenced by Kiley et al. (see, e.g., the abstract), Shirai et al. teaches that which is set forth in the above rejection of claims under 35 U.S.C. § 102(b). Moreover, Shirai et al. teaches that the fusion protein encoded by the "fused" nucleic acid molecule has the functionality of both PKC and GFP; see, e.g., the abstract. Shirai et al. teaches the nucleic acid molecule can be introduced into a mammalian host cell to monitor specific subcellular localization and translocation within the cell; see, e.g., the abstract. Shirai et al. teaches the studies have been used to clarify the different biological functions of different subspecies of PKC; see, e.g., page 411, column 2.

It would have been *prima facie* obvious to one ordinarily skilled in the art at the time of the invention to have produced a "fused" nucleic acid molecule comprising a polynucleotide sequence encoding the "Pnck" polypeptide, according to the Gardner et al., adjoined to a polynucleotide sequence encoding GFP, according to Shirai et al., because Shirai et al. teaches such a nucleic acid molecule can be used to produce a fusion protein in a mammalian cell to monitor specific subcellular localization and translocation of a cancer-linked protein kinase within the cell. One ordinarily skilled in the art would have been motivated to do so in order to clarify the biological function of the "Pnck" polypeptide in the

a mammalian cell, because Shirai et al. teaches monitoring specific subcellular localization and translocation of cancer-linked protein kinases within the cell to clarify their biological functions.

25. Claims 39, 40, 42, and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Database GenBank™ Accession No. AB023027 (04 December 1999), as evidenced by the USPTO search report "us-10-032-254a-2.rge", pages 1 and 2 of the "Alignments" (result 1), in view of Bendig (*Genet. Eng.* 1988; (7): 91-127), as evidenced by Lehninger et al. (Principles of Biochemistry, 2nd Ed., Worth Publishers: New York, 1993, pages 984-995).

Claims 39 and 44 are drawn to a recombinant mammalian cell comprising a nucleic acid molecule according to claim 3. Claim 40 is drawn to a vector comprising a nucleotide sequence according to claim 3. Claim 42 is drawn to a nucleic acid molecule that comprises a polynucleotide sequence that is complementary to all or part of a nucleic acid sequence according to claim 3.

Lehninger et al. teaches that cloned DNA molecules of which plasmids are comprised are double-stranded DNA molecules comprised of two DNA strands, each having a polynucleotide sequence that fully complementary to the other; see the entirety of pages 984-995 (e.g., page 994, Figure 28-9).

As evidenced by the USPTO search report, Database GenBank™ Accession No. AB023027 teaches that which is set forth above in the rejection of claim 3 under 35 U.S.C. § 102(b).

However, Database GenBank™ Accession No. AB023027, and the annotations set forth there under, do not expressly teach a recombinant cell or a mammalian cell comprising the disclosed nucleic acid molecule (claims 39 and 44, respectively); nor does the reference expressly teach a vector comprising the disclosed nucleotide sequence (claim 40), which is comprised of a nucleic acid molecule having a polynucleotide sequence that is complementary to the disclosed nucleic acid sequence (claim 42).

Bendig reviews the recombinant production of foreign proteins in mammalian cells; see entire document (e.g., the abstract). Bendig et al. teaches vectors comprising a polynucleotide sequence encoding a protein of interest are produced and introduced into mammalian host cells, which then produce the protein; see, e.g., the abstract.

As evidenced by Lehninger et al., the vectors described by Bendig, which encode the protein of interest, are double-stranded DNA molecules comprised of a DNA molecule comprising a polynucleotide sequence that is fully complementary to the polynucleotide sequence encoding the protein.

It would have been *prima facie* obvious to one ordinarily skilled in the art at the time of the invention to produce a vector comprising a polynucleotide sequence disclosed by Database GenBank™ Accession No. AB023027, which encodes a polypeptide that comprises an amino acid sequence that is identical to that set forth in the instant application as SEQ ID NO: 2, and then introduce the vector into a mammalian host cell. One ordinarily skilled in the art at the time of the invention would have been motivated to do so to produce the protein encoded by the polynucleotide sequence disclosed by Database GenBank™ Accession No. AB023027.

## ***Conclusion***

26. No claims are allowed.

27. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax

phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1642

slr
January 4, 2005